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DATA EVALUATION RECORD
(Addendum of June 3, 1993)

Study Type: Developmental Toxicity
Guideline §83-3
Species: Rabbit

EPA Identification No.s: EPA Accession No. 260966
EPA Pesticide Chemical Code: 128501
Toxicology Chemical Code: 893C

Test Material: SC-0224 (56.2% purity); Lot #EHC-0355-25. Note: Technical grade sulfosate is usually supplied as an aqueous solution. Because its viscous nature precludes the practical manufacture of a technical grade with a standard a.i. content (sulfosate froms an intractable glass-like product if its water content is ≤ 30%). From 1982 to the present time, the studies submitted to support registration had different a.i. contents ranging from 19.2 to 72%).

Synonyms: Trimethylsulfonium carboxymethylaminomethylphosphonate; sulfosate; Touchdown

Sponsor: Stauffer Chemical Co.

Study Number(s): T-11052

Testing Facility: Stauffer Chemical Co., Environmental Health Center, Farmington, CN

Title of Report: A Teratology Study in New Zealand White Rabbits with SC-0224.

Author(s): J. L. Minor and J. R. Downs

Report Issued: June 21, 1983

Conclusions: Sulfosate was administered by gavage to groups of mated New Zealand White rabbits (21 does in the highest dose group) on gestation days 7 through 19 at dose levels of 0, 10, 40, or 100 mg/kg/day. The test material was dissolved in water and administered in a volume of 2 ml/kg.

The maternal NOEL is 40 mg/kg/day according to the report, and the maternal LOEL is 100 mg/kg/day (6 deaths in 17 pregnant does, 4 abortions in the 11 survivors along with decreased body weight, feed consumption and body weight gain).

The developmental NOEL is 40 mg/kg/day and the LOEL is 100 mg/kg/day. This is based on the following: at 100 mg/kg/day, there was a reduction in the number of live fetuses/doe for the 7 surviving rabbits when compared with the controls (5.4 versus 7.4), 4 rabbits aborted their litters (apparently all of the fetuses were dead in those litters and if those are included in the calculations there would be a statistically significant decrease in live fetuses/doe and postimplantation loss), and having only 7 litters does not give a sufficiently high number of animals to absolutely conclude that no developmental toxicity is occurring, particularly in light of the massive losses to death and abortions.

Core Classification: Minimum.

This study satisfies the guideline requirements (§83-3) for a developmental toxicity study in rabbits.

Discussion: The original DER cited the increased incidence of clinical signs in the low dose group as the basis for setting the NOEL < 10 mg/kg/day (lowest dose tested). However, incidences reported (see table below, taken from Table 2 of the original report) indicate that those signs do not occur in a dose-related manner or in numbers that exceed control group values. It should also be noted that 4 of the 8 reported deaths appeared to be associated with dosing accidents (see attached Table 3 from the original report).

Attached Table 5 from the original report and the tables below summarize the effects of the test compound on body weight, weight change, and food consumption, and *in utero* results are summarized in the table below and in Table 7 in the Appendix.

All of these data suggest a maternal NOEL of 40 mg/kg/day and an LOEL of 100 mg/kg/day.

Data summarized in attached Tables 8, 9 and 10 from the original report indicate that possible developmental toxicity was observed at the highest dose tested (100 mg/kg/day).

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Clinical Signs for Does Gravid on Day 30

	Dose Levels (mg/kg/day)			
	0	10[a]	40	100
Females Examined	14	14	14	7
Without signs	13	7*	10	4
General				
Anorexia	0	0	1	2
Diarrhea	0	1	2	2
Lethargy	0	0	1	1
Head tilt	0	1	0	0
Nasal discharge after dosing	0	1	0	0
Wet stains, chin	0	1	0	0
Scab, mouth	0	1	0	0
Red urine	0	1	0	0
Red stains on cage pad	0	1	1	0
Respiratory				
Rales while dosing	1	0	0	0

*$p \leq 0.05$
[a]Each one of the clinical signs was observed in a different animal. No one animal in the 10 mg/kg/day dose group had more than 1 clinical sign.

Body Weight Gains (Kg)[a]

Group:	Prior to Dosing Period	Days 7 - 21	Days 21-30	Days 7 - 30	Corrected Body Weight Gain[1]
Control	0.3	0.2	0.0	0.2	-0.2
LDT	0.3	0.1	0.1	0.1	-0.3
MDT	0.3	0.1	0.1	0.2	-0.3
HDT	0.4	-0.3*	0.3*	0.0*	-0.4

[1]corrected body weight gain for entire gestation period = body weight gain for days 7 - 30 minus gravid uterus weight.
[a]Data extracted from table 5.
* $p < 0.05$

Food Consumption Data (g/day)[a]

	Days 0 - 7	Days 7 - 21	Days 21 - 30	Days 7 - 30
Group:				
Control	190	165	104	3200
LDT	191	136	119	2600
MDT	174	136	134	3000
HDT	199	54*	180	2000*

[a]Data extracted from table 5.
* $p < 0.05$

Cesarean Section Observations[a]

	Control	LDT	MDT	HDT
Dose (mg/kg/day)	0	10	40	100
# Animals Assigned	15	15	15	21
# Animals Mated/Inseminated	15	15	15	15
Pregnancy Rate (%)	14(93)	14(93)	14(93)	17(81)
Maternal Wastage				
# Died	0	0	0	8*[b]
# Died/pregnant	0	0	0	6
# Non pregnant	1	1	1	4
# Aborted	0	0	0	4*
# Dams with live fetuses	14	13	14	7
Total Corpora Lutea	119	132	113	73[c]
Corpora Lutea/dam	8.5	9.4	8.1	8.0
Total Implantation	117	103	104	133[d]
Implantations/Dam	8.4	7.4	7.4	7.1[d]
Total Live Fetuses	103	86	100	38
Live Fetuses/Dam	7.4	6.6	7.2	5.4[d]
Total Resorptions	14	17	4	12
Early	8	3	3	6
Mid	3	1	0	1
Late	3	13	1	5
Resorptions/Dam	1.0	1.3	0.3	1.7
Total Dead Fetuses	0	0	0	0
Dead Fetuses/Dam	0	0	0	0
Mean Fetal Weight (gm)	43	47	46	48
Preimplantation Loss(%)	2	22*	6	9
Postimplantation Loss(%)	12	6	4	22[d]
Standard Deviation	13	9	6	20
Sex Ratio (% Female)	56	60	56	61

[a]Data extracted from table 7.
* $p < 0.05$
[b]4 of 8 deaths were from dosing accidents.
[c]Some of these data were not available.
[d]Implantation sites were found in 17 dams. Later, only 7 dams had litters to term. If the values include the 4 females which aborted, then the following would values would be used: implants/dam - 7.6 ± 1.6, live fetuses/dam - 3.4* ± 3.0 and postimplantation loss (%) - 49* ± 42.

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Subsequent Review

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Pages 5 through 9 are not included in this copy.

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